SYNOPSIS

(1) TITLE OF THE SYNOPSIS

"STUDIES ON ANTIDEPRESSANT DRUG-SURFACTANT SYSTEMS AND HYDROPHOBIC ORGANIC COMPOUND SURFACTANT INTERACTION."

(2) INTRODUCTION

The micellar and interfacial properties of amphiphilic drugs are of paramount importance in the pharmaceutical research. Many drug molecules are amphiphilic and self-associate in aqueous environment to form small aggregates. This surface-active behavior among many diverse classes of drugs has been reported and attempts have been made to correlate surface and biological activities [1-3]. The self-association of drug depends on the molecular structure of the drug, its concentration and the experimental conditions e.g., temperature, pH and salt concentration etc. [2, 4].

The antidepressant drugs are a family of structurally similar compounds possessing an almost planar tricyclic ring system and a short hydrocarbon chain carrying a terminal, charged nitrogen atom (Scheme I) [5-6].

In pharmacy, the interaction of small molecules with drugs is extensively studied. In this respect, many drugs, particularly those with local anesthetic, antidepressant, tranquillizer, and antibiotic actions, exert their activity by interaction with biological membranes, which can be considered as a complex form of amphiphilic bi-layers. Thus, a full knowledge of the mechanism of the interactions of drugs with other foreign materials is required before the actual application in human body. This is due to the fact that drugs are always used in the presence of a variety of additives [7-9].

The first generation of a tricyclic antidepressant drugs suffers from several drawbacks like cardiovascular, anticholinergic and antiarrythymic side effects [10]. The

antidepressants are used along with a drug carrier, to minimize such effects. Surfactants are considered as good carriers as they form micelles and can solubilize drugs in their core. Drug molecules possess capacity of self-aggregation in aqueous medium, hence study of mixed micellization involving these types of drugs and surfactants have been of great advantage in pharmaceutical fields [11-16].

The solubility of biologically active compounds is often a limiting factor for their applicability. Solubility enhancement of drugs is an important task in pharmaceutical technology because it leads to better bioavailability. To process the solubilization by surfactants, known to form micelles, has been extensively studied [17-18]. An additional advantage of micelles as drug carriers from the practical point of view is that they are easy to prepare on a large scale [19-20].

Surfactants have particular significance in pharmacy due to their ability to increase the solubility of sparingly soluble substances in water [21-22].

Hydrophobic organic compounds are ubiquitous soil pollutants and cause many environmental problems [23]. Physical, chemical and biological methods have been used for the remediation of hydrophobic organic compounds contaminated sites. Many of the persistent contaminants especially polycyclic aromatic hydrocarbons (PAHs) exhibit low water solubility and hence, solubility of PAH can be improved by addition of surfactants, thereby facilitating transport across cell membranes and making them available for the degradation [24-25].

In the present work a systematic investigation on the physicochemical properties of some antidepressant drugs and their interaction with various surfactants will be attempted.

(3) REVIEW OF THE EARLIER WORK

Several studies [15-18] have been focused on physicochemical properties of drugs. Mosquera and group [20] have studied surface properties of some amphiphilic

antidepressent drugs. Thermodynamic studies on mixed micellization of amphiphilic drug amitriptyline hydrochloride and nonionic surfactant Triton X-100 have been studied by Mandal and group [1]. Effect of aditive on poorly water-soluble drugs studied by Akers and co-workers [26]. The surface and micellar properties of some amphiphilic drugs in the presence of additives and the conductometric study of antidepressent drug-cationic surfactant mixed micelles in aqueous solution has been studied by Kabir-ud-Din et al. [3,9,19]. In these studies the drug /surfactant system shows an increase in synergism with the increase in surfactant concentraion. The result indicates that with increase in the conccentration of surfactants the cmc values of drugs decreases.

In recent years, it was observed that micellar solutions of the surfactant obtained significantly improved the solubility of hydrophobic drugs with respect to pure water, by inducing these molecules in the hydrophobic micellar core, as well as protected them from degradation [27-31]. The micellar solubilization of drugs has been studied by Carlota et al. [32]. The result obtained showed that the solubilization of drugs increases early with the increasing surfactant concentration because of the association between the drugs and the micelles. A study on solubilization of poorly soluble drugs by cyclodextrins and micelles has been done by Gokturk et al. [33]. This study shows that the aqueous solubility of poorly soluble drugs can considerably be improved by micellar solubilization. The solubilization of some cationic, anionic, and nonionic surfactants towards the poorly water-soluble drug has been studied by Rather and group [34]. In this work the cationic surfactant showed the highest molar solubilization capacity. The effect of polymeric additives on the solubilization of a poorly-soluble drug in micellar solutions have studied by Attwood [35]. Udawat et al. [36] studied the micellar solubilization of poorly- water soluble drug using nonionic surfactant. Cheema et al. [37] studied the surface and bulk properties of antidepressant drugs. A number of studies [2-9] on micellar solubilization of poorly water soluble drugs have been done in recent years. Study of thermodynamics of amphiphilic drug imipramine hydrochloride in presence of additives has been done by Mandal and group [38]. Recently Mahajan et al. [39-40]

studied the interfacial, micellar and spectroscopic properties of some antidepressant drugs in the presence of ionic surfactant.

Solubilization behavior of different organic compounds in the micellar system has studied by several workers [21-23]. Many laboratories have been conducted the interactions with surfactant type composition and concentration [41-56]. Chun et al. [57] studied the solubilization of PAH mixture by three different anionic surfactants. Dar et al. [45] studied the solubilization capabilities of mixtures of cationic gemini surfactant with conventional cationic, nonionic, anionic surfactants towards polycyclic aromatic hydrocarbons. Recently Kabir-ud-Din and group [47] studied the solubilization of PAHs by novel biodegradable cationic gemini surfactant ethane-1, 2-diyl bis (N, N-dimethyl-N-hexadecylammoniumacetoxy) dichloride and its binary mixtures with conventional surfactants. Investigation on solubilization of polycyclic aromatic hydrocarbons in the presence of single and mixed gemini surfactants has been studied by Huang et al. [48]. Paria and group [58] studied the solubilization of Naphthalene by pure and mixed surfactants. Ghosh et al. [59] studied the solubility efficiency of polycyclic aromatic hydrocarbons in single surfactant systems.

(4) OBJECTICVES OF THE STUDY

The specific objectives of the present investigation are:

I. To study the surface and micellar properties of some amphiphilic antidepressant drugs by conductometric, tensiometric and fluorimetric methods.

II. To determine the interaction parameter of amphiphilic drugs in the presence of single and mixed surfactants.

III. To characterize the solubilization of drugs in the presence of surfactants.

IV. To study the influence of surfactants on the solubilization of some hydrophobic organic compounds.

(5) NOTEWORTHY CONTRIBUTIONS

Antidepressant drugs are widely used in treating psychiatric and neurologic disorder. Over the year many classes of antidepressants have been used in India and all over the world. The excess amount of drugs can cause overstimulation, psychotic illness and other disorders. So the targeted drug delivery in body organs with surfactants and other system is necessary. In order to use these systems as drug carrier, a detailed study of drug-surfactant interaction as well as the effect of microenvironment is prerequite. This field is very much important for biochemical application and drug delivery system.

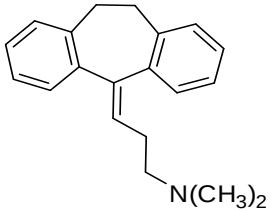
Surfactants have numerous applications in various fields. These compounds are also used to solubilizeand mobilize many environmental hazardous and toxic pollutants like polycyclic aromatic hydrocarbons from the contaminated sites.

(6) PROPOSED METHODOLOGY OF THE RESEARCH WORK

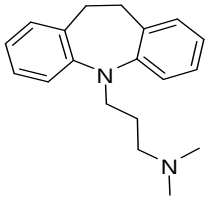
The entire experimental work will be done in the following steps:

I. To study the surface and micellar properties of some amphiphilic antidepressant drugs by conductometric, tensiometric and fluorimetric methods.

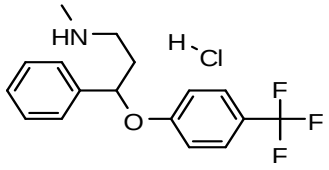
The physicochemical properties of some amphiphilic drugs (Scheme I) will be determined by conductometric, tensiometric and fluorimetric methods. The critical micelle concentration (CMC), degree of micellar ionization, maximum surface excess concentration at the air/water interface (Γ_{max}), minimum area per surfactant molecule at the air-water interface (A_{min}) and the surface pressure at the CMC (π_{CMC}) will be determined.



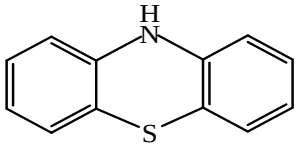
Amitriptyline



Imipramine



Fluoxetine hydrochloride

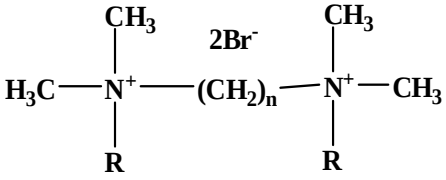


Phenothizine

Scheme I. Structures of Amphiphilic Drugs

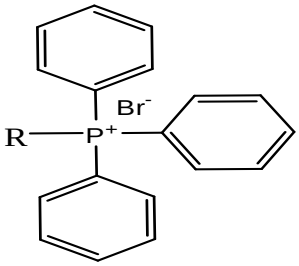
II. To determine the interaction parameter of amphiphilic drugs in the presences single and mixed surfactants.

Some interaction parameters i.e. critical micelle concentration (CMC_{exp}, CMC_{ideal}), micellar mole fraction (X_1 and X_{ideal}), interaction prarmeters (β), activity coefficients (f_1 and f_2) and excess Gibb's free energy (ΔG^E) will be determined. Various cationic, anionic, non-ionic and gemini surfactants (Scheme II) will be used.



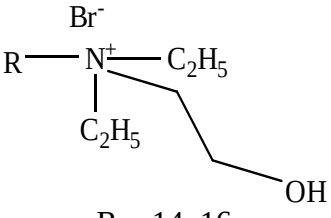
n = 3, 4, 6, 10, 12

Quaternary ammonium gemini surfactant



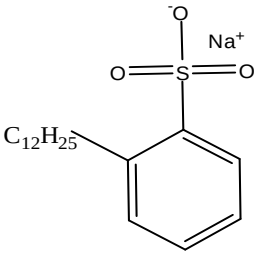
R = 14, 16

Alkyltriphenylphosphonium bromide

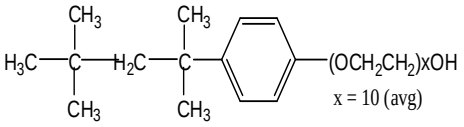


R = 14, 16

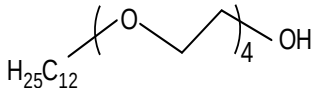
Alkyldiethylethanolammonium bromide



Sodium dodecyl benzene suphonate



Triton X-100



Brij-35

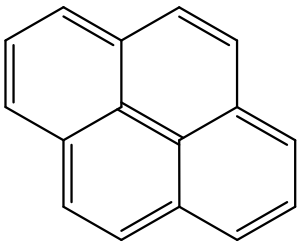
Scheme II Structure of Surfactants

III. To characterize the solubilization of drugs in the presence of surfactants.

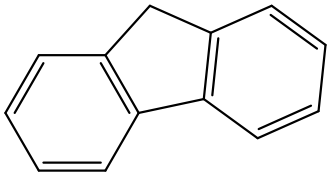
Solubilization of amphiphilic drugs will be studied in surfactants systems. Quantification of solubilization capacity has been undertaken in terms of the molar solubilization ratio (MSR), the micellar water partition coefficient (ln K_m) and Gibb's free energy of solubilization ($\Delta G°_s$) by employing spectrophotometric method.

IV. To study the influence of surfactants on the solubilization of some hydrophobic organic compounds.

Solubilization of hydrophobic organic compounds will be studied in surfactants systems. Quantification of solubilization capacity has been undertaken in terms of the molar solubilization ratio (MSR), the micellar water partition coefficient (ln K_m) and Gibb's free energy of solubilization ($\Delta G°_s$) by employing spectrophotometric method.



Pyrene



Fluorene

Scheme III Structure of PAHs

(7) EXPECTED OUTCOME OF THE PROPOSED WORK

The studies of micelles in drug delivery yield the necessary information to minimize drug degradation, loss and prevent harmful side effects with increased drug bioavailability. The use of micelle in pharmacy is an important tool that finds numerous applications. Special emphasis will be given to the more recent use of polymeric micelles.

Most of the drugs are used in combination with additives specially surfactants. Therefore, it is necessary to have knowledge of the additive effect on the cmc of amphiphilic drugs. The micellar and interfacial properties will very useful for the development of new drugs.

A comprehensive fundamental investigation would advance our understanding of surfactant behavior. The present study will investigate the solubilization behavior of PAHs (Polycyclic Aromatic Hydrocarbons) by surfactant system. Solubility of PAH in water is greatly enhanced in a linear fashion. The experiment results of present study can be used to understand the water-solubility enhancements of organic pollutants by surfactant can extend the scope of contaminant remediation.

Polycyclic aromatic hydrocarbons are toxic pollutants and have been of great environmental concerns.Surfactant induced solubilization of such PAHs can greatly enhance contaminant transport and recovery. The contamination of soils and groundwater by toxic and hazardous organic pollutants is a widespread environmental problem. Surfactant can increase the aqueous solubility of non-aqueous phase liquids and the dissolution of soil bound aromatic hydrocarbon.

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(9) **LIST OF PAPER PUBLISHED IN JOURNAL:**

I. Study of Solubility Efficiency of Polycyclic Aromatic Hydrocarbons in Single Surfactant Systems. Jyotsna Lakra, Deepti Tikariha, Toshikee Yadav, Manmohan L. Satnami, Kallol K. Ghosh. J. Surf. Deterg., (**2013**). DOI 10.1007/s11743-013-1507-8.

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